REMARKS

Claims 42, 45 and 55-70 are pending in the subject application. Applicants have herein amended claim 42. Support in the specification for amended claim 42 is set forth in the table below.

Amended Claim 42	Support in Specification
A method for treating a disease involving β-sheet fibril formation in a subject which comprises administering to the subject	Page 26, lines 15-20; page 39, lines 30-32
an amount of a soluble compound which comprises a V-domain of RAGE	Page 27, lines 29-31 and page 28, line 1; page 28, lines 10-12
effective to inhibit binding of the β-sheet fibril to receptor for advanced glycation endproduct,	Page 26, lines 17-19; page 40, lines 1 and 2
wherein the β-sheet fibril comprises amylin, amyloid A, transthyretin, cystatin C, or gelsolin,	Page 26, lines 24-26

so as to thereby treat the disease involving β-sheet fibril formation in the subject.	Page 26, lines 19 and 20; page 40, lines 2-4

Applicants have also canceled claims 45, 55-58, and 62-69 without disclaimer or prejudice to their right to pursue the subject matter of these claims in the future.

Applicants have also added new claims 71-79. Support in the specification for new claims 71-79 can be found in the table below.

Claim	Support in Specification
71. The method of claim 42, wherein the soluble compound comprises the V-domain of RAGE linked to an antibody or a portion of an antibody.	Page 27, line 29-31; page 28, lines 1; page 42, line 3
72. The method of claim 42, wherein the soluble compound comprises the V-domain of RAGE linked to a portion of an antibody.	Page 27, line 29-31; page 28, lines 1; page 42, lines 3 and 4
73. The method of claim 42, wherein the portion of the antibody is a F_{ab} fragment.	Page 42, lines 6 and 7

74. The method of claim 42, wherein the portion of the antibody is an F_c fragment.	Page 42, lines 6-8
75. The method of claim 42, wherein the β-sheet fibril comprises amylin.	Page 26, lines 24 and 25
76. The method of claim 42, wherein the β-sheet fibril comprises amyloid A.	Page 26, lines 24 and 25
77. The method of claim 42, wherein the β-sheet fibril comprises transthyretin.	Page 26, lines 24 and 25
78. The method of claim 42, wherein the β-sheet fibril comprises cystatin C.	Page 26, lines 24-26
79. The method of claim 42, wherein the β-sheet fibril comprises gelsolin.	Page 26, lines 24-26

Applicants maintain that this Amendment raises no issue of new matter. Accordingly, upon entry of this Amendment, claims 42 (as amended), 59-63 and 70-79 will be pending and under examination in the subject application.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 42, 45, 55-57 and 59-70 under

35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner alleged that the phrase "a compound other than sRAGE, which compound (i) comprises a fragment of sRAGE and (ii) is capable of inhibiting binding of the β-sheet fibril to RAGE" as recited in previously pending claim 42 is new matter.

In response, to advance prosecution but without conceding the correctness of the rejection, applicants note that claims 45, 55-58 and 62-69 have been canceled herein without disclaimer or prejudice. Accordingly, the Examiner's rejection of these claims is moot.

In response to the rejection of claim 42, as well as claims 59-63 and 70 which are dependent thereon, applicants note that amended claim 42 does not recite "a compound other than sRAGE, which compound (i) comprises a fragment of sRAGE and (ii) is capable of inhibiting binding of the β-sheet fibril to RAGE." Rather, claim 42, as amended, provides, in relevant part, "an amount of a soluble compound which comprises the V-domain of RAGE." As indicated in the table above, support for amended claim 42 can be found in the specification at, *inter alia*, page 26, lines 15-20; page 39, lines 30-32; page 27, lines 29-31 and page 28, line 1; page 28, lines 10-12; page 26, lines 17-19; page 40, lines 1 and 2; page 26, lines 24-26; page 26, lines 19 and 20; and page 40, lines 2-4

Accordingly, applicants maintain that amended claim 42, and

dependent claims 59-61 and 70, are fully supported by the specification as filed.

In view of the amendment to claim 42 and the preceding remarks, applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, first paragraph.

Double Patenting Rejection

The Examiner maintained the provisional rejection of claims 42, 45 and 55-70 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-3 and 16 of copending U.S. Serial No. 08/905,709, now U.S. Patent No. 7,101,838, issued September 5, 2006 ("the '838 patent"), and claims 36, 39, 40 and 53 of copending U.S. Serial No. 09/498,459.

Applicants note that U.S. Serial No. 08/905,709 has issued and is now the '838 patent. Claim 1 of the '838 patent recites a "method of inhibiting atherosclerosis in a subject suffering from hyperlipidemia which comprises administering to the subject a polypeptide which comprises a soluble extracellular portion of a receptor for advanced glycation endproduct (sRAGE) capable of inhibiting an interaction between amyloid-β peptide and receptor for advanced glycation endproduct (RAGE) in an amount effective to inhibit atherosclerosis in the subject," and claims 2-9 of the '838 patent are dependent thereon.

Applicants further note that claims 36, 39, 40 and 53 of copending U.S. Serial No. 09/498,459 were canceled and replaced with new claims 56-62. New independent claim 56 recites a "method for treating a subject afflicted with atherosclerosis which comprises administering to the subject an agent capable of inhibiting the interaction of amyloid-β peptide with receptor for advanced glycation end product, the agent being present in an amount sufficient to inhibit amyloid-β peptide interaction with the receptor for advanced glycation end product on the subject's cells, thereby treating atherosclerosis in the subject," and claims 57-62 are dependent thereon.

Applicants understand the Examiner's provisional double-patenting rejection to be based on the issued claims of the '838 patent, insofar as they correspond to previously pending claims 1-3 and 16, and the pending claims in U.S. Serial No. 09/498,459, insofar as they correspond to previously pending claims 36, 39, 40 and 53.

In response to the provisional rejection of claims 45, 55-58, and 62-69, and without conceding the correctness of the Examiner's rejection, applicants note that these claims have been canceled herein. Accordingly, the Examiner's rejection thereof is moot.

In response to the rejection of claim 42, as well as claims 59-63 and 70 which are dependent thereon, applicants note that claim 42 has been amended such that its subject matter is patentably distinct from that of the issued claims of

U.S. Patent No. 7,101,838, and the pending claims of U.S. Serial No. 09/498,459.

Specifically, applicants note that claim 42, as amended, provides, in part, a method comprising administering to the subject an amount of a soluble compound which comprises a V-domain of RAGE effective to inhibit binding of a β-sheet fibril to receptor for advanced glycation endproduct, wherein the β-sheet fibril comprises amylin, amyloid A, transthyretin, cystatin C, or gelsolin.

Applicants note that the claims of the '838 patent do not recite the inhibition of a β-sheet fibril to receptor for advanced glycation endproduct, wherein the β-sheet fibril comprises amylin, amyloid A, transthyretin, cystatin C, or gelsolin. Applicants further note that the claims of U.S. Serial No. 09/498,459 do not recite the inhibition of a β-sheet fibril to receptor for advanced glycation endproduct, wherein the β-sheet fibril comprises amylin, amyloid A, transthyretin, cystatin C, or gelsolin. Therefore, such claims do not anticipate or render obvious amended claim 42. Accordingly, claims 42, 59-61 and 70 in the subject application are not obvious over the claims of U.S. Patent No. 7,101,838 and U.S. Serial No. 09/498,459.

In order to ensure compliance with 37 C.F.R. §1.56, applicants direct the Examiner's attention to U.S. Serial No. 11/805,164, filed May 21, 2007, which is a continuation of U.S. Serial No. 09/374,213, the benefit of which is claimed in the subject application. The claims now pending

in U.S. Serial No. 11/805,164 are attached as Exhibit A hereto and are also submitted in the Supplemental Information Disclosure Statement incorporated herein.

In view of amended claim 42 and the preceding remarks, applicants respectfully request that the Examiner reconsider and withdraw the provisional double-patenting rejection based on the '709 application (now '838 patent) and the '459 application.

Rejections under 35 U.S.C. §102(b)

The Examiner rejected claims 42, 45, 55, 57, 59-61, 63-68 and 70 under 35 U.S.C. §102(b) as allegedly anticipated by WO 97/26913 ("the '913 application").

Specifically, the Examiner alleges that the '913 application teaches a method for treating a subject with a condition associated with the interaction of an amyloid-β peptide with RAGE, which comprises administering to the subject an agent capable of inhibiting the interaction between amyloid β-peptide and RAGE, the agent being present in an amount effective to inhibit the interaction between amyloid β-peptide and RAGE, thereby treating the subject. The Examiner further alleges that the condition may be any of a number of disorders, such as diabetes, renal failure, hyperlipidemic atherosclerosis, ALS, neuronal cytotoxicity, MS, Down's syndrome and neuronal degeneration, which the Examiner asserts may be associated with amyloid β-peptide fibril or with aggregation of amyloid β-peptide fibrils.

In response to the rejection of claims 45, 55, 57, and 63-68, and without conceding the correctness of the Examiner's rejection, applicants note that these claims have been canceled herein. Accordingly, the Examiner's rejection of these claims is moot.

In response to the rejection of the remaining claims, applicants respectfully traverse.

Applicants note that claim 42, as amended, recites a method for treating a disease involving β-sheet fibril formation in a subject which comprises administering to the subject an amount of a soluble compound which comprises a V-domain of RAGE effective to inhibit binding of the β-sheet fibril to receptor for advanced glycation endproduct, wherein the β-sheet fibril comprises amylin, amyloid A, transthyretin, cystatin C, or gelsolin, so as to thereby treat a disease involving β-sheet fibril formation in the subject.

Applicants note that the '913 application does not teach β-sheet fibrils which comprise amylin, amyloid A, transthyretin, cystatin C, or gelsolin, as recited in amended claim 42. Accordingly, applicants maintain that amended claim 42, and dependent claims 59-61, and 70, are not anticipated by the '913 application.

In addition, applicants hereby expressly withdraw and disclaim all arguments previously made with respect to the '913 application. Upon reflection such arguments were misplaced.

The Examiner also rejected claims 42, 45, 55, 57, 59-68 and 70 under 35 U.S.C. §102(e) as allegedly anticipated by Morser, U.S. Patent No. 5,864,018 ("the '018 patent).

Specifically, the Examiner alleges that the '018 patent discloses a method for inhibiting atherosclerotic plaque formation in a diabetic subject, which comprises administering to said subject a polypeptide which comprises sRAGE or a derivative thereof, said polypeptide being capable of inhibiting the interaction between amyloid β-peptide and RAGE. Therefore, a compound capable of blocking interaction of amyloid β-peptide would inherently be capable of blocking the interaction of a β-sheet fibril and RAGE.

In response to the rejection of claims 45, 55, 57, and 62-68 applicants note that these claims have been canceled herein. Accordingly, the Examiner's rejection of these claims is moot.

In response to the rejection of the remaining claims, applicants respectfully traverse.

Applicants again note that claim 42, as amended, recites a method for treating a disease involving β-sheet fibril formation in a subject which comprises administering to the subject an amount of a soluble compound which comprises a V-domain of RAGE effective to inhibit binding of the β-sheet fibril to receptor for advanced glycation endproduct,

wherein the β-sheet fibril comprises amylin, amyloid A, transthyretin, cystatin C, or gelsolin, so as to thereby treat a disease involving β-sheet fibril formation in the subject.

Applicants note that the '018 application does not teach β-sheet fibrils which comprise amylin, amyloid A, transthyretin, cystatin C, or gelsolin, as provided in amended claim 42. Accordingly, applicants maintain that amended claim 42, and dependent claims 59-61 and 70, are not anticipated by the '913 application.

In view of amended claim 42 and the preceding remarks, applicants respectfully request that the Examiner reconsider and withdraw his rejection under 35 U.S.C. §102(b).

Rejection under 35 U.S.C. §103(a)

The Examiner also rejected claims 42, 45 and 55-57 and 59-70 under 35 U.S.C. §103(a) as allegedly obvious over the '018 patent, in view of Lilley, et al. and further in view of Kelly.

In response to the rejection of claims 45, 55-57, and 62-69, applicants note that these claims have been canceled herein. Accordingly, the Examiner's rejection of these claims is moot.

In response to the rejection of claims 42 and 59-61, and

70, applicants respectfully traverse.

The teachings of the '018 patent are discussed above in applicants' preceding remarks regarding the 35 U.S.C. §102 rejection.

Applicants again note that the '018 application does not teach or suggest β-sheet fibrils which comprise amylin, amyloid A, transthyretin, cystatin C, or gelsolin, as provided in amended claim 42.

Lilley, et al., which teach that diabetes mellitus is associated with delayed wound healing, and Kelly, et al., which teach that prion diseases result from β-sheet fibril formation, fail to cure the deficiency of the '018 patent, in that neither reference teaches or suggests a method involving β-sheet fibril which comprise amylin, amyloid A, transthyretin, cystatin C, or gelsolin.

Accordingly, applicants maintain that no combination of the cited references teaches or suggests all the elements of the now claimed invention. Therefore, amended claim 42, and dependent claims 59-61 and 70, are not obvious over the '018 patent, in view of Lilley, et al. and further in view of Kelly.

In view of amended claim 42 and the preceding remarks, applicants respectfully request that the Examiner reconsider and withdraw his rejection under 35 U.S.C. §103(a).

Supplemental Information Disclosure Statement

This Supplemental Information Disclosure Statement is submitted to supplement the Information Disclosure Statements filed September 20, 2002 and May 10, 2005.

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on the PTO-1449 form attached hereto as **Exhibit B**.

1. U.S. Patent No. 6,100,098, issued August 8, 2000 to Newkirk;

2. U.S. Patent No. 6,465,422, issued October 15, 2002 to Schmidt, et al.

3. PCT Publication No. WO 98/44955, published October 15, 1998 on behalf of Mindset Ltd., et al. (**Exhibit 1**);

4. PCT Publication No. WO 97/39121, published October 23, 1997 on behalf of Morser, et al. (**Exhibit 2**);

5. Hale, K. et al. "Multifunctional Regulation of the Biological Effects of TNF-α by the Soluble Type I and Type II TNF Receptors," Cytokine 7(1):26-38 (1995) (**Exhibit 3**);

6. Hardy, J. "The Alzheimer family of diseases: Many etiologies, one pathogenesis?" PNAS 90:2095-2097 (1997) (**Exhibit 4**);

7. Heaney, M., et al. "Soluble Hormone Receptors," Blood 82(7):1945-1948 (1993) (**Exhibit 5**);

8. Hsiao, K., et al. "Correlative Memory Deficits, Aβ Elevation, and Amyloid Plaques in Transgenic Mice," Science 274:99-102 (1996) (**Exhibit 6**);

9. Miyata, T., et al. "The Receptor for Advanced Glycation End Products (RAGE) is a Central Mediator of the Interaction of AGE-β2 Microglobulin with Human Mononuclear Phagocytes via an Oxidant-sensitive Pathway," J. Clin. Invest. 98(5):1088-1094 (1996) (**Exhibit 7**);

10. Picciotto, M., "Using Knockout and Transgenic Mice to Study Neurophysiology and Behavior," Physiol. Review 78:1131-1163 (1998) (**Exhibit 8**);

11. Schenk, D., et al., "Immunization with amyloid-β attenuates Alzheimer-disease-like pathology in the PDAPP mouse," Nature 400:173-177 (1999) (**Exhibit 9**);

12. Weggen, et al., "A subset of NSAIDs lower amyloidogenic Aβ42 independently of cyclooxygenase activity," Nature 414:212-216 (2001) (**Exhibit 10**); and

13. Claims 41-53 currently pending in U.S. Application No. 11/805,164, filed May 21, 2007, of David M. Stern, et al. (**Exhibit 11**).

Above-listed references 1 and 2 are U.S. patents. Accordingly, under 37 C.F.R. §1.98(a)(2)(ii), copies of these references are not required to be provided to the U.S. Patent and Trademark Office.

Applicant requests that the Examiner consider these references, initial the attached Form PTO-1449 and make the references of record in the subject application.

Summary

In view of the amendments to claim 42 and the preceding remarks, applicants maintain that the pending claims are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed sum of §690.00, including the $510.00 fee for a three-month extension of time and the $180.00 fee for filing a Supplemental Information Disclosure Statement, is deemed necessary in connection with the filing of this Amendment. However, if any

additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

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John P. White
Reg. No. 28,678

Date

EXHIBIT A

Applicants: David Stern et al.
U.S. Serial No.: 10/049,893
Filed: July 22, 2002

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

1-40. (Canceled)

41. (New) A method of inhibiting binding of a β-sheet fibril to a receptor for advanced glycation endproduct on the surface of a cell of a subject which comprises administering to the subject an amount of a soluble compound which comprises a V-domain of RAGE effective to inhibit binding of the β-sheet fibril to receptor for advanced glycation endproduct, wherein the β-sheet fibril comprises amylin, amyloid A, prion-derived peptide, transthyretin, cystatin C, or gelsolin.

42. (New) The method of claim 41, wherein the soluble compound is sRAGE.

43. (New) The method of claim 41, wherein the soluble compound is a fragment of sRAGE which comprises the V-domain of RAGE.

44. (New) The method of claim 41, wherein the soluble compound is linked to an antibody or portion of an antibody.

45. (New) The method of claim 44, wherein the portion of the antibody is a F_{ab} fragment.

46. (New) The method of claim 44, wherein the portion of the antibody is an F_c fragment.

47. (New) The method of claim 41, wherein the cell is a neuronal cell, an endothelial cell, a glial cell, a microglial cell, a smooth muscle cell, a somatic cell, a bone marrow cell, a liver cell, an intestinal cell, a germ cell, a myocyte, a mononuclear phagocyte, a tumor cell, or a stem cell.

48. (New) The method of claim 41, wherein the β-sheet fibril comprises amylin.

49. (New) The method of claim 41, wherein the β-sheet fibril comprises amyloid A.

50. (New) The method of claim 41, wherein the β-sheet fibril comprises prion-derived peptide.

51. (New) The method of claim 41, wherein the β-sheet fibril comprises transthyretin.

52. (New) The method of claim 41, wherein the β-sheet fibril comprises cystatin C.

53. (New) The method of claim 41, wherein the β-sheet fibril comprises gelsolin.

EXHIBIT B

Applicants: David Stern et al.
U.S. Serial No.: 10/049,893
Filed: July 22, 2002